Achievement of Hba1c targets in the Diabetes Unmet Need with basal insulin Evaluation (DUNE) real-world study

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INTRODUCTION

- Treatment guidelines advocate the achievement of individualized Hba1c targets to reduce the glycaemic burden in people with type 2 diabetes (T2DM).1

- Approximately half of all people with T2DM are unable to achieve glycaemic targets (Hba1c < 7.0% [53 mmol/mol]) in clinical practice, with even lower rates for those treated with basal insulin.1

- In addition, non-treatment with basal insulin is associated with suboptimal long-term blood glucose control.4

- In insulin-treated people with T2DM, suboptimal glycaemic control may be due, in part, to non-adherence to basal insulin therapy and/or dose reduction in the setting of a fear of hypoglycaemia.6,10

- The association between achievement of individualized glycaemic targets and hypoglycaemia risk in the real-world setting is unknown.

OBJECTIVE

- To assess individualized Hba1c target achievement and its potential association with the occurrence, frequency, and severity of symptomatic hypoglycaemia in a real-world setting.

METHODS

- **Design:** The Diabetes Unmet Need with basal Insulin Evaluation (DUNE) study was a 12-week, single-arm, prospective, observational study (February 2015 to July 2016).

- **Study population:**
  - Key inclusion criteria: Age ≥18 years and having T2DM in people either newly initiated with BI at the time of enrolment, or treated with BI for <12 months (previously initiated) with or without oral antihyperglycaemic drug and/or glucagon-like peptide-1 receptor agonists.
  - Hba1c >7.5% [53 mmol/mol] for newly initiated BI users, and 7.5% to 10.0% [57 mmol/mol to 86 mmol/mol] for previously initiated BI users.
  - Key exclusion criteria: Treatment with rapid-acting or premix insulin or physician plans to initiate treatment with a rapid-acting or premix insulin within the next 3 months.

- **Primary endpoints:**
  - Achievement of individual Hba1c target at 12 weeks (if an individual target is not defined at baseline, a general Hba1c target of <7.5% [53 mmol/mol] will be considered as relevant).
  - The impact of symptomatic hypoglycaemia according to its frequency and severity on short-term Hba1c target achievement at 12 weeks.

- **Secondary endpoints:**
  - Achievement of the general Hba1c target of <7.0% [53 mmol/mol] and <8.0% [64 mmol/mol] at week 12, according to level of risk of hypoglycaemia complications.1
  - Hba1c and basal insulin dose changes from baseline.
  - Hypoglycaemia—any symptomatic, severe, and documented symptomatic events (glycemic: ketonuria; creatinine >54 cmol/L [7.9 mmol/L] and 3.9 mmol/L).1

- **Data analysis and statistics:**
  - The relationship between achievement of individualized Hba1c targets at 12 weeks was summarised using a 95% confidence interval (95% CI).
  - The relationship between Hba1c target at 12 weeks and symptomatic hypoglycaemia was analysed using univariate and multivariate logistic regression.
  - The multivariate analysis was adjusted on the baseline characteristics of region, age, duration of diabetes, Hba1c, use of sulphonylureas and/or glitazones, and use of glucagon-like peptide-1 receptor agonists. Other factors included in the model were selected by stepwise analysis.

RESULTS

- **Study participants:** The evaluable study population included 3139 participants from 28 countries (Table 1).

- **Individualized Hba1c target:** Of the evaluable participants, 97.9% were set individualized Hba1c targets by their physician (3.1% did not set individualized targets but were assigned a general target of <7.0% [53 mmol/mol]) (Figure 1).

- **Achievement of Hba1c target at 12 weeks:** Of the evaluable participants, 27.4% of participants achieved their individualized physician-defined Hba1c targets ([1–4] Figure 2). Only 23.5% of participants from the newly initiated group and 20.2% from the previously initiated group achieved their individualized Hba1c targets at 7.0% to 7.5% [53.0 to 58.5 mmol/mol]) (Figure 1).

- **Change in basal insulin dose and Hba1c, from baseline to week 12:** At week 12 both newly and previously initiated participants showed a mean Hba1c decrease from baseline with modest up- titration of insulin dose (Table 2).

- **Self-reported hypoglycaemia:**
  - Symptomatic hypoglycaemia was experienced by 18.3% and 14.2% of previously and newly initiated participants, respectively (Table 3).

- **The incidence of severe hypoglycaemia during the study was low (1.7% for previously and newly initiated participants, respectively) (Table 3).**

DISCUSSION

- **DUNE benefitted from a large, real-world population, with a comprehensive collection of patient characteristics.**

- **Most participants did not achieve individualized Hba1c targets set by their physician.**

- **The short study duration may have contributed to a lower than expected rate of hypoglycaemia (1.3% overall), and impacted on the associations with target achievement.**

- **While it has previously been suggested that hypoglycaemia may negatively impact the achievement of Hba1c targets, this was not observed in this study.**

- **The modest dose increase observed suggests that there is an opportunity for people with T2DM and their physicians to titrate insulin more effectively.**

- **Further studies are required to better understand the reasons behind the lack of insulin titration and why many individuals with T2Dm do not achieve Hba1c targets in the real-world setting.**

CONCLUSIONS

- **Results from this real-world study showed that while Hba1c levels fell substantially, most participants did not achieve individualized Hba1c targets (mostly 7.0–7.5%).**

- **Participants who reached Hba1c targets were more likely to experience 0–1 symptomatic hypoglycaemic events.**

Table 1: Demographic and baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Newly initiated (n=1716)</th>
<th>Previously initiated (n=1423)</th>
<th>All (n=3139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>68.6 (11.2)</td>
<td>60.3 (10.3)</td>
<td>67.0 (11.0)</td>
</tr>
<tr>
<td>Gender, female, %</td>
<td>49.6</td>
<td>53.4</td>
<td>51.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.9 (5.8)</td>
<td>26.8 (5.1)</td>
<td>27.3 (5.5)</td>
</tr>
<tr>
<td>Mean Hba1c, %</td>
<td>9.3 (1.0)</td>
<td>10.0 (1.3)</td>
<td>9.8 (1.1)</td>
</tr>
<tr>
<td>Mean change in Hba1c vs. baseline, %</td>
<td>0.37 (0.14)</td>
<td>0.30 (0.13)</td>
<td>0.34 (0.13)</td>
</tr>
</tbody>
</table>

Table 2: Change in basal insulin dose and Hba1c, from baseline to week 12

<table>
<thead>
<tr>
<th>Variable</th>
<th>Newly initiated (n=1716)</th>
<th>Previously initiated (n=1423)</th>
<th>All (n=3139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily insulin dose (kg)</td>
<td>27.9 (10.9)</td>
<td>25.4 (11.1)</td>
<td>26.7 (10.8)</td>
</tr>
<tr>
<td>Change</td>
<td>2.1 (1.0)</td>
<td>1.8 (0.9)</td>
<td>2.0 (1.0)</td>
</tr>
</tbody>
</table>

Table 3: Self-reported hypoglycaemic events

<table>
<thead>
<tr>
<th>Variable</th>
<th>Newly initiated (n=1716)</th>
<th>Previously initiated (n=1423)</th>
<th>All (n=3139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic hypoglycaemic events</td>
<td>1.4 (1.4)</td>
<td>1.3 (1.3)</td>
<td>1.3 (1.3)</td>
</tr>
<tr>
<td>Frequency of symptomatic hypoglycaemic events, % participants</td>
<td>11.0</td>
<td>10.3</td>
<td>10.7</td>
</tr>
<tr>
<td>Number of symptomatic hypoglycaemic events</td>
<td>2.6 (0.6)</td>
<td>2.3 (0.5)</td>
<td>2.5 (0.6)</td>
</tr>
</tbody>
</table>

**Table 4: Multivariate logistic regression model of self-reported hypoglycaemic events at 12 weeks**

**DISCUSSION**

**Table 5: Side effects, adverse events, and laboratory parameters at baseline (n=3139)**

- **Hba1c target achievement at 12 weeks:**
  - Univariate logistic regression analysis showed a positive association between the occurrence (OR=0.001) and frequency (OR=0.004) of symptomatic hypoglycaemia and Hba1c target achievement.
  - Adjusting on baseline characteristics, the multivariate analysis demonstrated a significant positive impact on the occurrence of symptomatic hypoglycaemia, and Hba1c target achievement (Table 4).
  - Participants who experienced ≥2 symptomatic events were more likely to achieve their Hba1c target compared to those who experienced 0–1 symptomatic hypoglycaemic events (Table 4).

- **RESULTS**

- **FUNDING:**
  - **DISCLOSURES:**

- **REFERENCES:**

- **CONTACT DETAILS:**

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